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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/478,567

01/06/2000

A. Gurraj Rao

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04/08/2004

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EXAMINER

KALLIS, RUSSELL

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/478,567

Applicant(s)

RAO ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/14/2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5-12 and 14-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-12 and 14-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-3, 5-12, and 14-20 are examined. Claims 4 and 13 are cancelled.

The rejection of Claims 18-20 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of Applicant's amendments.

Specification

The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Figures 1, 2, and 4 describe VSP sequences that each must have a sequence identifier. Correction is required.

Claim Rejections - 35 USC § 112

Claims 1-3, 5-12 and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The added claimed material which is not supported by the original disclosure is as follows: Newly amended Claims 1 and 8 recite "by at least one essential amino acid residue" while the specification only supports "significantly higher levels of methionine in lines 26-27 of page 2; "the proteins can be designed to be enriched in essential amino acids . . . relative to average levels of such amino acids" in lines 27-30 on page 3, and an increased essential amino acid content within the protein of at least about 5%, 10%, 20% or 40% of the total amino acid

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content on page 7, lines 25-32 and page 8, line 1. Further, there is no support for "by at least one essential amino acid residue" in the originally filed claims of Application 08/988,015 filed 12/10/97. Support cannot be found on the pages Applicant indicated. Applicant is invited to point to the page and line number in the specification where support can be found. Absent of such support, Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1-3, 5-12, and 14-20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant asserts that the specification provides exemplary nucleotide and amino acid sequences as well as guidance regarding the evaluation of the functional limitations of the claims (response page 8). The claims are drawn to nucleic acid molecules encoding engineered proteins having increased essential amino acid content. Applicant does not describe a representative number of exemplary nucleic acid molecules that define the genus of sequence having increased essential amino acid content as broadly claimed. There is insufficient relevant identifying characteristics to allow one of skill in the art to predictably determine the structure of other nucleic acid molecules absent further guidance.

Claims 1-3, 5-12, and 14-20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

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was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant asserts that the specification provides exemplary guidance for evaluation of the functional limitations of the claims (response page 9). Applicant teaches methionine enriched variant VSP β -10 binding to wild type VSP β specific antibodies (page 19) which only suggest that VSP β -met10 may be correctly folded in an *E. coli* secretion system as stated by Applicant in the specification on page 20, lines 1-2. This does not meet required level of certainty as recited in the limitation of Claims 1 and 8 "retains the conformation of the native protein and therefore binds". Further, Applicant has not addressed the Examiner's statements in the enablement rejection directed towards the limitations of monoclonal antibodies in discriminating against non-native or non-corresponding VSP β variants. Moreover, the results Applicant recites on page 19 of the specification do not indicate any background binding as relative control. Furthermore, no guidance is provided for making an engineered protein having an altered amino acid composition that would bind to a modified protein that binds to a native protein. It is uncertain which alteration would be compatible with the other alterations and how one would assay for productive binding. Nonetheless, undue experimentation would be required to make, clone, and express a multitude of non-exemplified variants of a nucleic acid molecule encoding a protein engineered for an increase in the level of essential amino acids, that binds with an antibody or protein molecule that also binds with a native form of the engineered protein and would require one of skill in the art to test in a myriad of non-exemplified plants for expression. Therefore, the invention is not enabled.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-12, and 14-20 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 1, and throughout the claims, “at least about” is indefinite because it sets a lower limit but “about” can be below that limit. Therefore, the metes and bounds are unclear.

At Claim 1 and 8, “capable of binding” is indefinite. It is unclear if the binding is specific or non-specific or under what conditions binding would occur. It is suggested that “capable of” be deleted.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. In the present instance, Claims 1 and 8 recite the broad recitation “an engineered protein comprising an amino acid sequence which differs from the amino acid sequence of a native protein by at least one essential amino acid residue”, and the claims also recite “wherein said engineered protein has an altered amino acid composition in comparison to said native protein, wherein said altered amino acid composition comprises an increase in essential amino acid content to be at least about 5%”, which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless --

(c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 5-11, 14 and 17-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Jung R. *et al.* WO 97/35023 published September 25, 1997.

The claims read on any transgenic plant transformed with any polynucleotide altered to encode a protein engineered to have increased essential amino acid changes (i.e. methionine and cysteine) and that differs from the amino acid sequence of a native VSP α or VSP β protein by at least one essential amino acid residue, and that binds in any fashion with any antibody or any protein, as does the corresponding native VSP α or VSP β protein.

The claims are broadly drawn to soybean plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have at least one essential amino acid increased to 10% of total amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

Jung teaches an isolated soybean 2S Albumin protein cDNA (Example 2 page 32); an isolated soybean 2S Albumin protein cDNA engineered (Albumin 1/3) to have 13.14% lysine and 12.4% methionine and cysteine (Example 3 pages 35-36); transformation of soybean plants transformed with cDNA encoding modified soybean 2S Albumin, a vegetative seed protein, said engineered peptides and seeds thereof (Example 4 pages 37-42); and preparation of Albumin specific antibodies that bind to both native and engineered soybean 2S Albumin proteins (Example 4 pages 42-43). Thus, the reference teaches all the limitations of Claims 1-3, 5-11, 14 and 17-18.

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Claims 1-3, 5-12, 15-16 and 18-20 remain rejected under 35 U.S.C. 102(e) as being anticipated by Tarczynski M. *et al.* U.S. Patent 6,080,913 filed September 25, 1996.

The claims read on any transgenic plant transformed with any polynucleotide altered to encode a protein engineered to have increased essential amino acid changes (i.e. methionine and cysteine) and that differs from the amino acid sequence of a native VSP α or VSP β protein by at least one essential amino acid residue, and that binds in any fashion with any antibody or any protein, as does the corresponding native VSP α or VSP β protein.

The claims are drawn to maize and soybean plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have at least one essential amino acid increased to 10% of total amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

Tarczynski teaches transformation of maize with an engineered cDNA from barley encoding a high lysine derivative of alpha-hordothione and plants having 20% or more of the target amino acid (see Claims 1, 9-11, 14-15, 17 and 19-22), a seed vegetative storage protein, targeted to the seed (Example III columns 13-14); and an endoplasmic reticulum targeting sequence KDEL for retention in the ER of maize that interacts with the proteins of the ER as do the corresponding native maize proteins. Thus the reference teaches all the limitations of Claims 1-3, 5-12, 15-16 and 18-20.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5-11, 14-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Jung R. *et al.* WO 97/35023 published September 25, 1997 in view of Gordon-Kamm *et al.* The Plant Cell, July 1990; Vol. 2; pp. 603-608.

The claims are drawn to soybean and maize plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have an essential amino acid increased to 10% of total protein amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

The teachings of Jung are discussed *supra*.

Jung does not teach Maize transformation.

Gordon-Kamm *et al.* teach transformation of maize (pages 615-616).

It would have been obvious at the time of Applicant's invention to modify the invention of Jung to include a method for transformation of maize. One of skill in the art would have been motivated by the knowledge common in the art that the method of maize transformation as taught by Gordon-Kamm *et al.* is valuable for genetic engineering of plants to enhance the amino acid profile of a plant by expression of an engineered protein as taught by Jung *et al.* are and given the success of Gordon-Kamm in the expression of exogenous genes in Maize and Jung in expression of amino acid enhanced peptides in soybean, one would have had a reasonable expectation of success of expressing genes encoding amino acid enhanced peptides in transformed maize plants and plant cells.

No Claim is allowed.

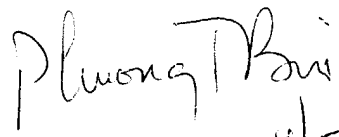
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
March 30, 2004


PHUONG T. BUI
PRIMARY EXAMINER
4/5/04